

FIG. 1A

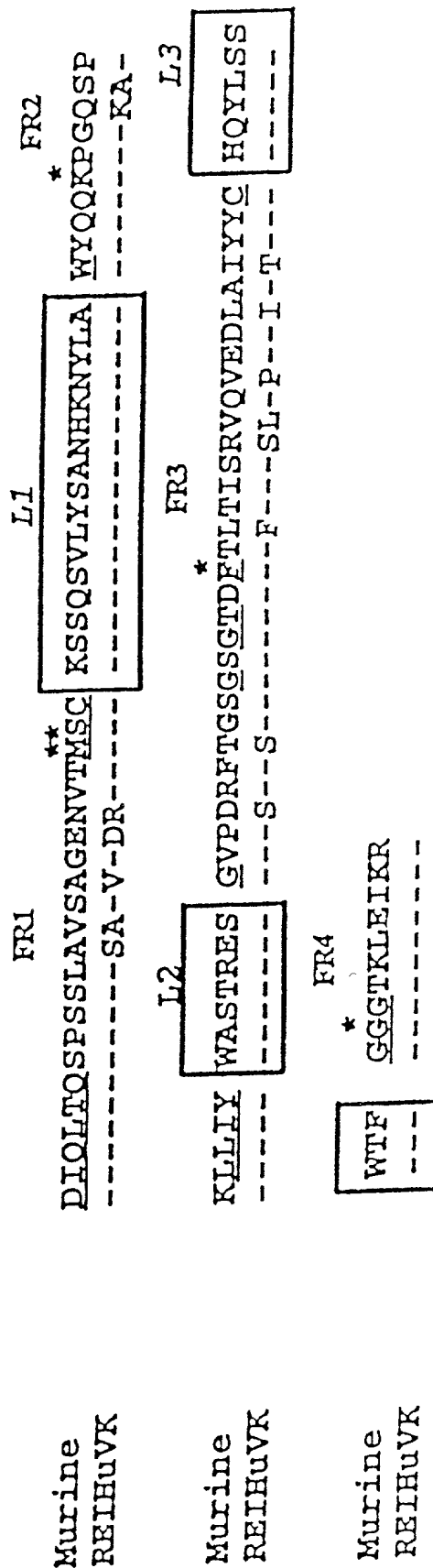


FIG. 1B

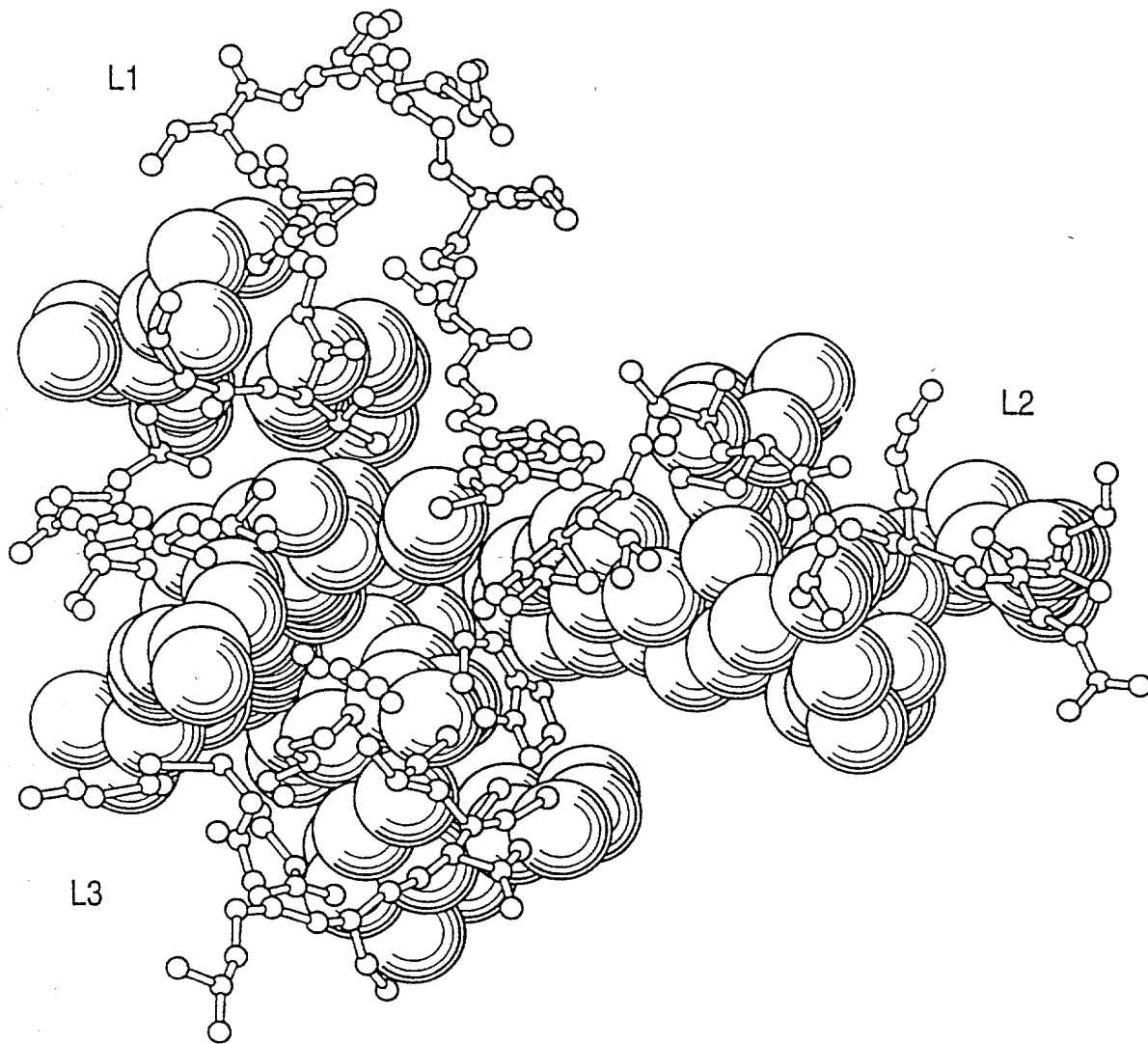
Murine	FR1	*	*	H1	FR2	*
EUHuVH1	QVQLQESGAELSKPGASVKMSCKASGYTFT			SYWLH	WIKQRPQGGLFWIG	
EUHuVH2	---Q---VK---S---V---V---			---	--VR-A---	
	---VQ---VK---S---V---			---	--VR-A---	
Murine	H2	**		FR3	*	
EUHuVH1	YINPRNDYTEYNQNEKD			KATLTADKSSSTAYMQLSSLTSEDSAVYYCAR		
EUHuVH2	---			---I---E-TN---E---R---T-F-F---		
	---			---I---E-TN---E---R---T-F-F---		
Murine	H3		FR4			
NEWMHuVH1	RDITTFY		WGQGTTLTVSS			
NEWMHuVH2	---		V			
	---		V			

Title: IMMUNOCONJUGATES AND
HUMANIZED ANTIBODIES SPECIFIC
FOR B-CELL LYMPHOMA AND
LEUKEMIA CELLS

Inventor(s): Shui-on LEUNG et al.

Appl. No.: 09/741,843

FIG. 2A



09/741,843

100240" E48T460
Title. IMMUNOCONJUGATES AND
HUMANIZED ANTIBODIES SPECIFIC
FOR B-CELL LYMPHOMA AND
LEUKEMIA CELLS

Inventor(s): Shui-on LEUNG et al.

Appl. No.: 09/741,843

FIG. 2B

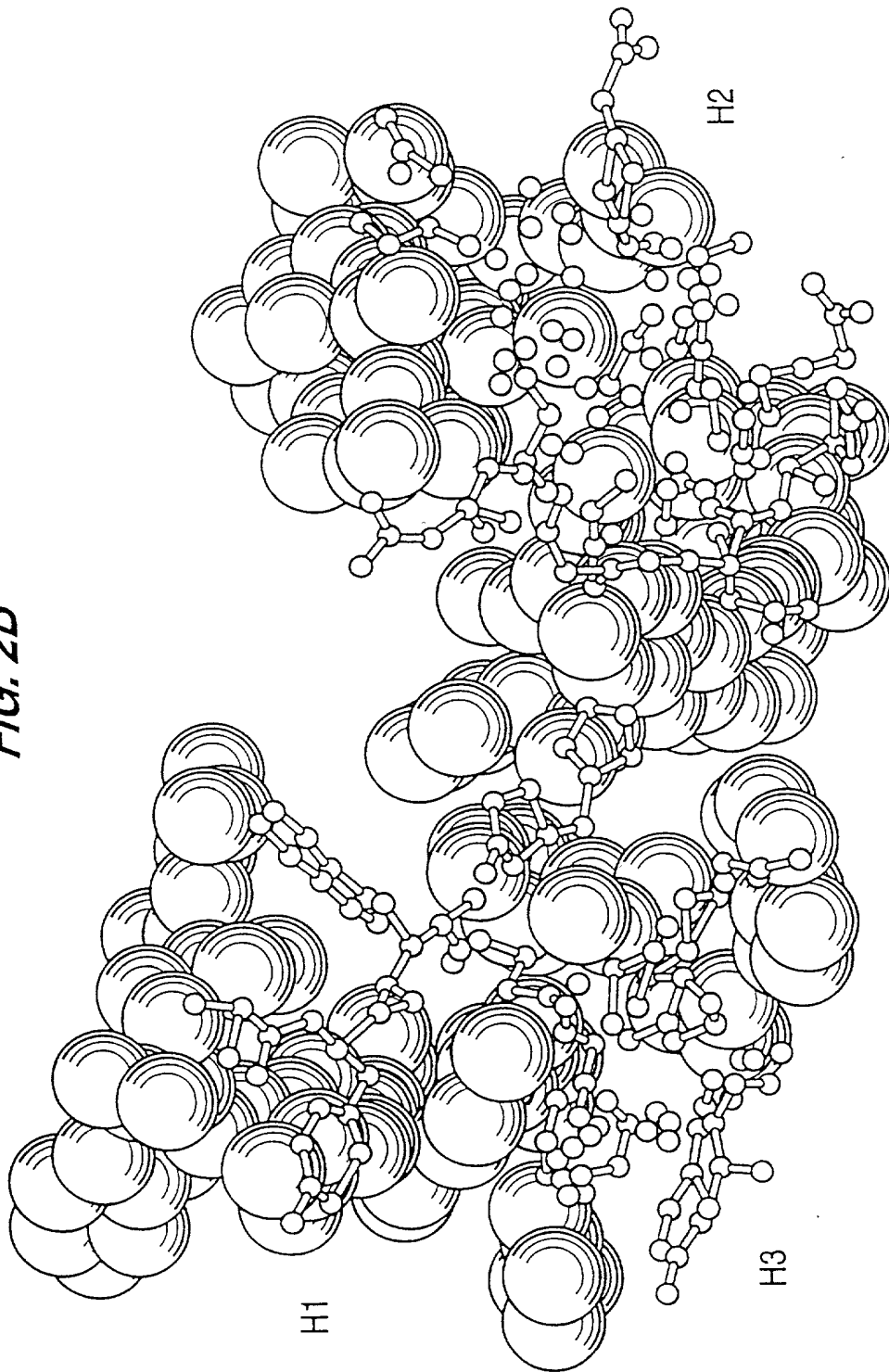


FIG. 3A

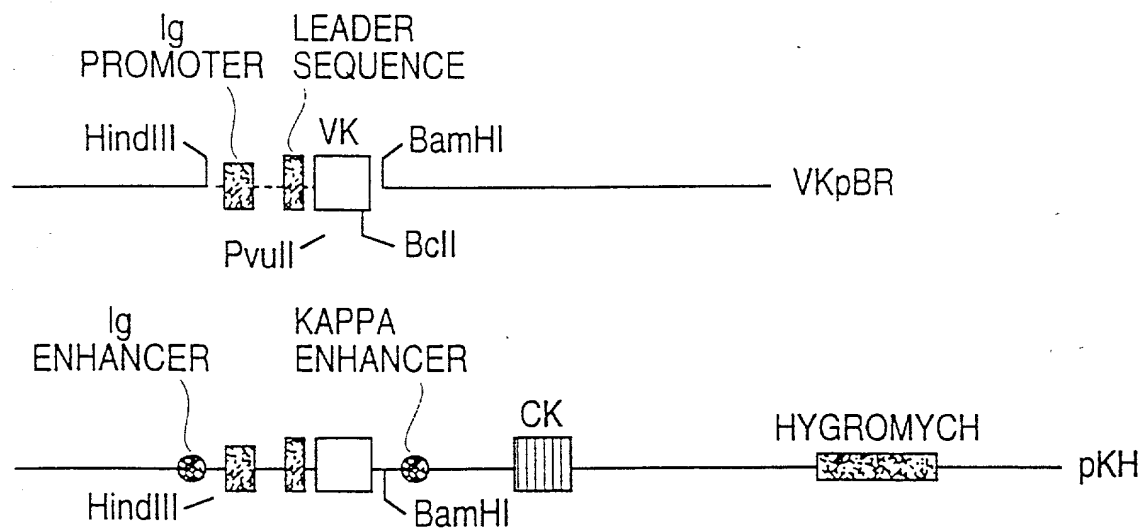
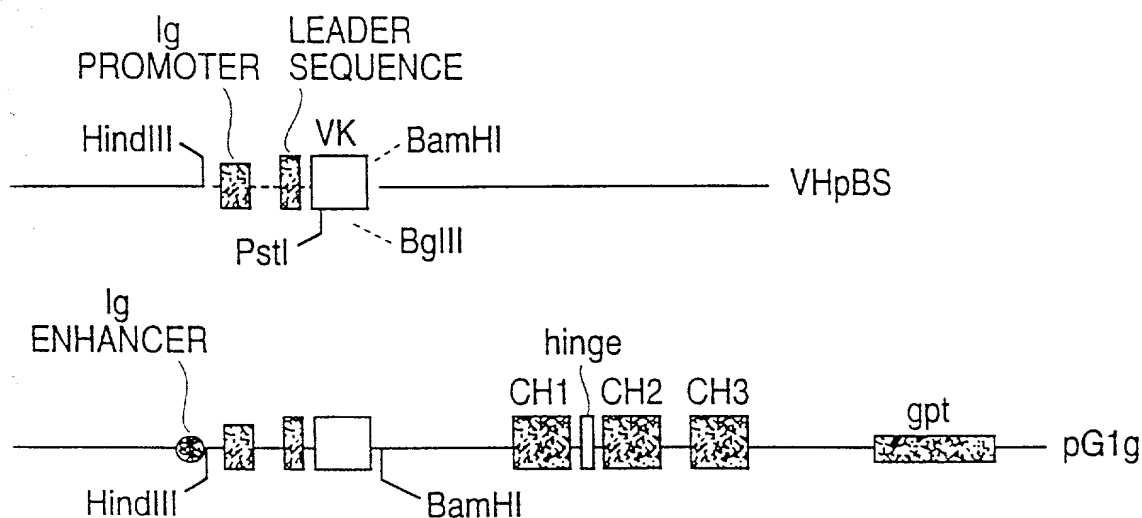


FIG. 3B



1	GACATTCAGCTGACCCAGTCTCCATCATCTCTGGCTGTGTCTGCAGGAGAAACGTCAC	60
	CTGTAAGTCGACTGGGTCAGAGGTAGTAGAGACCGACACAGACGTCCTCTTTTGCAGTGA	
	D I Q L T Q S P S L A V S A G E N V T	
61	ATGAGCTGTAAGTCCAGTCAAAAGTGTTTATACAGTGCAAAATCAACAAGAACTACTTGGCC	120
	TACTCGACATTCAGGTCAGTTTCACAAAATATATGTCACGTTAGTGTCTTGTGATGAACCGG	
	CDR1	
	M S C K S S Q S V L Y S A N H K N Y L A	
121	TGGTACCAGCAGAAACACGGGCAGTCTCCTAAACTGCTGATCTACTGGGCATCCACTAGG	180
	ACCATGGTCGCTCTTGGTCCCGTCAGAGGATTTGACGACTAGATGACCCGTAGGTGATCC	
	CDR2	
	W Y Q Q K P G Q S P K L L I Y W A S T R	
181	GAATCTGGTGTCCCTGATCGCTTCACAGGCAGCGGATCTGGGACAGATTTTACTCTTACC	240
	CTTAGACCACAGGACTAGCGAAGTGTCGGTCGCCCTAGACCCCTGTCTAAAATGAGAAATGG	
	E S G V P D R F T G S G S G T D F T L T	
241	ATCAGCAGAGTACAAGTTGAAGACCTGGCAATTATATTGTCACCAATACCTCTCCTCG	300
	TAGTCGTCTCATGTTCAACTTCTGGACCGTTAAATAATAACAGTGTATTGAGAGGAGC	
	CDR3	
	I S R V Q V E D L A I Y Y C H Q Y L S S	
301	TGGACGTTTCGGTGGAGGGACCAAGCTGGAGATCAAAACGT	339
	ACCTGCAAGCCACCTCCCTGGTTCGACCTCTAGTTTGCA	
	W T F G G G T K L E I K R	

CAGGTCCAGCTGCAGGAGTCAGGGGCTGAACCTGTCAAAAACCTGGGGCCTCAGTGAAGATG
 1-----+-----+-----+-----+-----+-----+-----+-----+ 60
 GTCCAGGTCGACGTCCTCAGTCCCGGACTTGACAGTTTGGACCCCGGAGTCACCTCTCTAC
 Q V Q L Q E S G A E L S K P G A S V K M -
 TCCTGCAAGGCTTCTGGCTACACCTTTACTAGCTACTGGCTGCACTGGATAAAACAGAGG
 61-----+-----+-----+-----+-----+-----+-----+-----+ 120
 AGGACGTTCCGAAGACCGATGTGGAAATGATCGATGACCGACGTGACCTATTTTGTCTCTCC
 CDR1
 S C K A S G Y T F T S Y W L H W I K Q R -
 CCTGGACAGGGTCTGGAAATGGATTGGATACATTAATCCTAGGAATGATTATACTAGGTAC
 121-----+-----+-----+-----+-----+-----+-----+-----+ 180
 GGACCTGTCCAGACCTTACCTAACCTATGTAATTAGGATCCTTACTAATATGACTCATG
 CDR2
 P G Q G L E W I G Y I N P R N D Y T E Y -
 AATCAGAACTTCAAGGACAAGGCCACATTGACTGCAGACAAATCCTCCAGCACAGCCTAC
 181-----+-----+-----+-----+-----+-----+-----+-----+ 240
 TTAGTCTTGAAGTTCTCTGTTCCGGTGTAACCTGACGTCGTGTTAGGAGGTCGTGTCGGATG
N Q N F K D K A T L T A D K S S T A Y -
 241-----+-----+-----+-----+-----+-----+-----+-----+ 300
 ATGCAACTGAGCAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAAGGGAT
 TACGTTGACTCGTCGGACTGTAGACTCCTGAGACGTCAGATAATGACACGTTCTTCCCTA
 M Q L S S L T S E D S A V Y Y C A R R D -
 ATTACTACGTTCTACTGGGGCCAAAGCACCACTCTCACAGTCTCCCTCG
 301-----+-----+-----+-----+-----+-----+-----+-----+ 348
 TAATGATGCAAGATGACCCCGGTTCCGTGGTGAGAGTGTACAGAGGAGC
 CDR3
 I T T F Y W G Q G T T L T V S S -

FIG. 5A

GACATTGAGCTGACCCAGTCTCCATCATCTCTGAGCGCATCTGTTGGAGATAGGGTCACT
 1-----+-----+-----+-----+-----+ 60
 CTGTAAGTCGACTGGGTCAGAGGTAGTAGAGACTCGGTAGACAACTCTATCCAGTGA
 D I Q L T Q S P S S L S A S V G D R V T -
 ATGAGCTGTAAGTCCAGTCAAAGTGTATTATACAGTGCAAATCACAAGAACTACTTTGGCC
 120
 TACTCGACATTCAGGTCAGTTTCACAAAATATGTCACGTTTAGTGTCTTGTGATGAACCGG
 CDR1
 M S C K S S Q S V L Y S A N H K N Y L A -
 TGGTACCAGCAGAAACCAGGGAAGCACCTAACTGCTGATCTACTGGGCATCCACTAGG
 180
 121 ACCATGGTCGCTTTGGTCCCTTTTCGTGGATTGACGACTAGATGACCCGTAGGTGATCC
 CDR2
 W Y Q Q K P G K A P K L L I Y W A S T R -
 GAATCTGGTGTCCCTTCGCGATTCTCTGGCAGCGGATCTGGGACAGATTCTTACTTTCACC
 240
 181 CTTAGACCCACAGGAAGCGCTAAGAGACCGTCGCCCTAGACCCCTGCTAAATGAAAGTGG
 E S G V P S R F S G S G S G T D F T F T -
 ATCAGCTCTCTCAACCAGAGACATTGCAACATATTATTGTCACCAATACCTCTCCCTCG
 241
 TAGTCGAGAGAAAGTTGGTCTTCTGTAAACGTTGTATAATAACAGTGGTTATGGAGAGGAGC
 CDR3
 I S S L Q P E D I A T Y Y C H Q Y L S S -
 TGGACGTTCCGGTGGAGGGACCAAGCTGGAGATCAAAACGT
 339
 301 ACCTGCAAGCCACCTCCCTGGTTCGACCTCTAGTTTGCA
 W T F G G G T K L E I K R

FIG. 5B

CAGGTCCAGCTGGTCCAATCAGGGGCTGAAGTCAAGAAACCTGGGTCAATCAGTGAAGGTC
 1 -----+-----+-----+-----+-----+ 60
 GTCCAGGTCGACACAGGTTAGTCCCGACTTCAGTTCTTTGGACCCAGTAGTCACTTCCAG

 Q V Q L V Q S G A E V K K P G S S V K V -
 TCCTGCAAGGCTTCTGGCTACACCTTTACTAGCTACTGGCTGCACTGGGTCAAGCAGGCA
 61 -----+-----+-----+-----+-----+ 120
 AGGACGTTCCGAAGACCGATGTGGAATGATCGATGACCGACGTGACCCAGTCCGTCCGT

 S C K A S G Y T F T S Y W L H W V R Q A -
 CCTGGACAGGCTCTGGAATGGATTGGATACATTAATCCTAGGAATGATTATTAAGTAC
 121 -----+-----+-----+-----+-----+ 180
 GGACCTGTCCCAGACCTTACCTAACCTATGTAATTAGGATCCTTACTAATAATGACTCATG

 P G Q G L E W I G Y I N P R N D Y T E Y -
 AATCAGAACTTCAAGGACAAGGCCACAATAACTGCAGACGAATCCACCAATACAGCCTAC
 181 -----+-----+-----+-----+-----+ 240
 TTAGTCTTGAAGTTCCTGTCCGGTGTATTGACGCTGCTAGGTGGTTATGTCGGATG

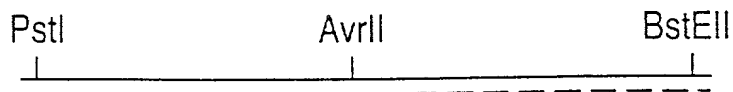
N Q N F K D K A T I T A D E S T N T A Y -
 ATGGAGCTGAGCAGCCTGAGGTCTGAGGACACGGCATTTTATTTTGTGCAAGAGGAT
 241 -----+-----+-----+-----+-----+ 300
 TACCTCGACTCGTCCGACTCCAGACTCCTGTGCCGTAAATAAAACACGTTCTTCCCTA

 M E L S S L R S E D T A F Y F C A R R D -
 ATTAAGTCTTACTGGGGCCAAGCACACCGTCAACGCTCTCCTCG
 301 -----+-----+-----+-----+-----+ 348
 TAATGATGCAAGATGACCCCGTTCCGTGGTCCAGTGGCAGAGGAGC

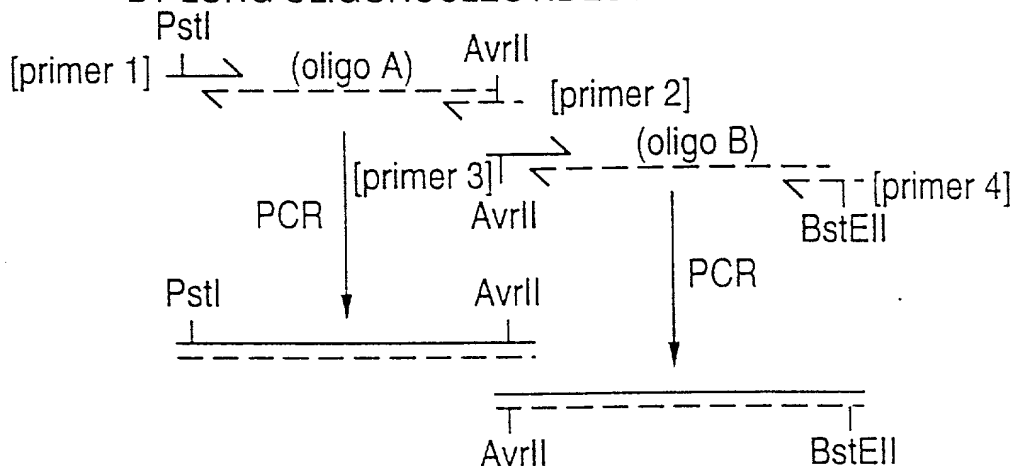
 CDR3
I T T F Y W G Q G T T V T V S S -

FIG. 6

DESIGNED SEQUENCE FOR HUMANIZED LL2 VH DOMAIN:



CONSTRUCTION OF THE HUMANIZED LL2 VH DOMAIN
BY LONG OLIGONUCLEOTIDES AND PCR:



PstI/AvrII DIGESTION

BstEII/AvrII DIGESTION

LIGATION TO THE PstI/BstEII
SITES OF THE HEAVY CHAIN
STAGING VECTOR: VHpBS

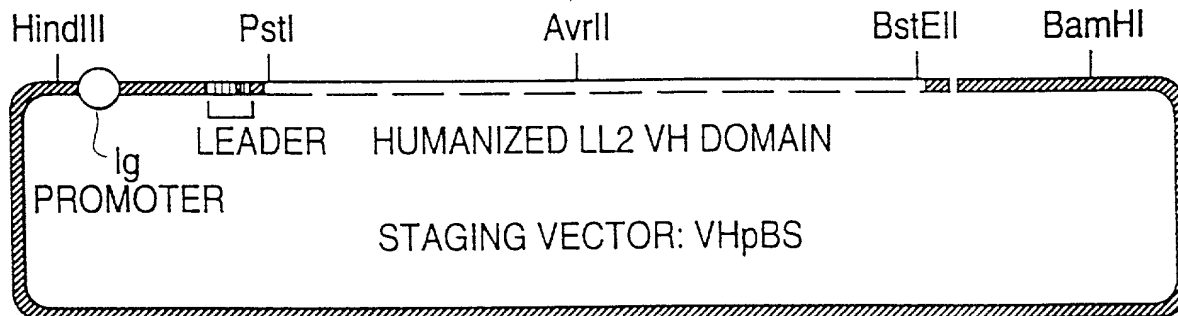


FIG. 7

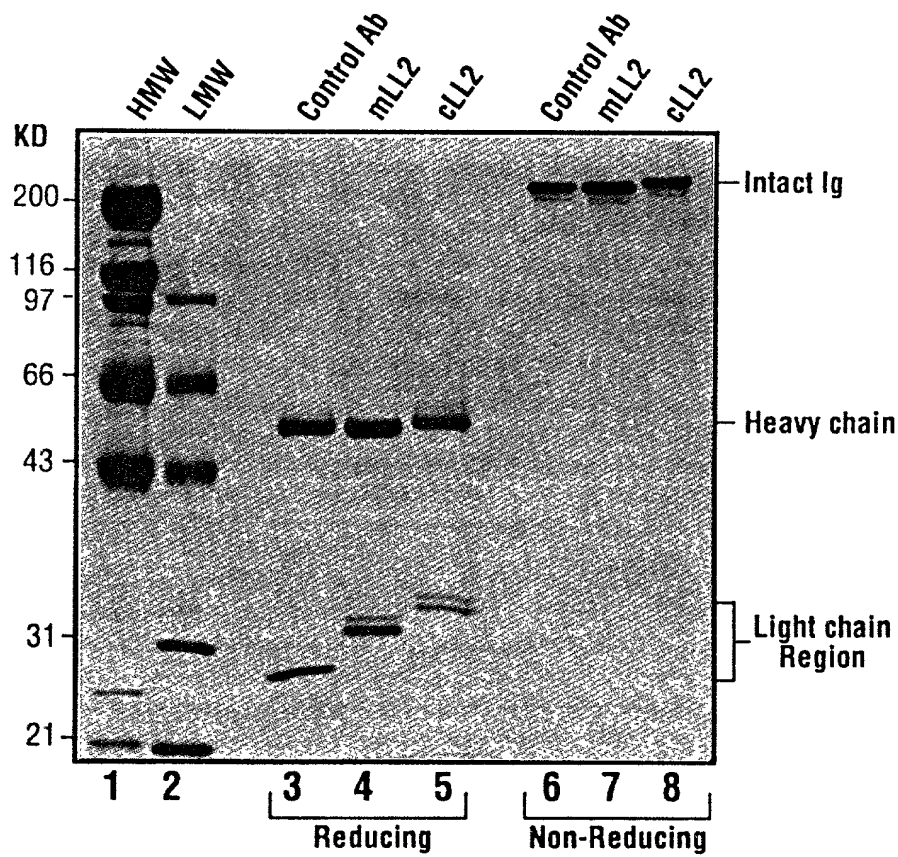


FIG. 8

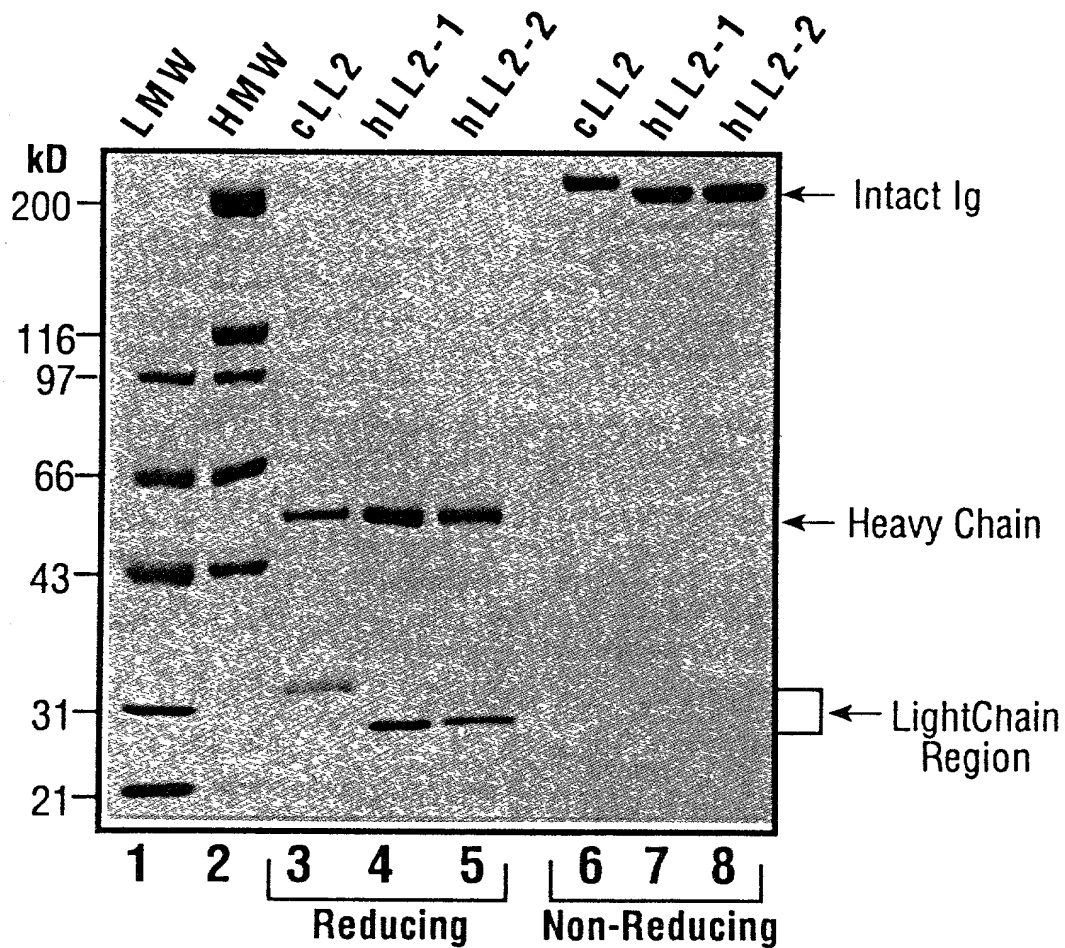


FIG. 9

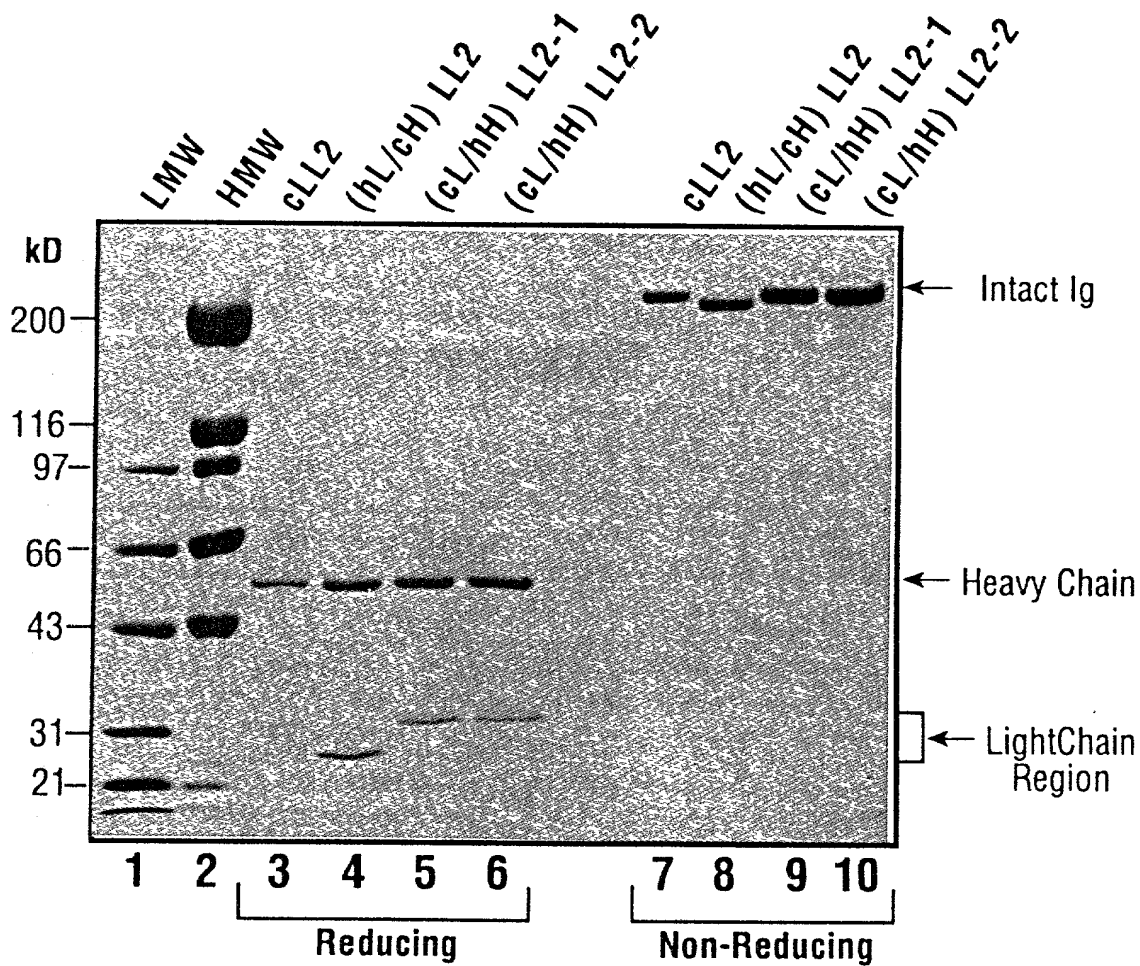


FIG. 10

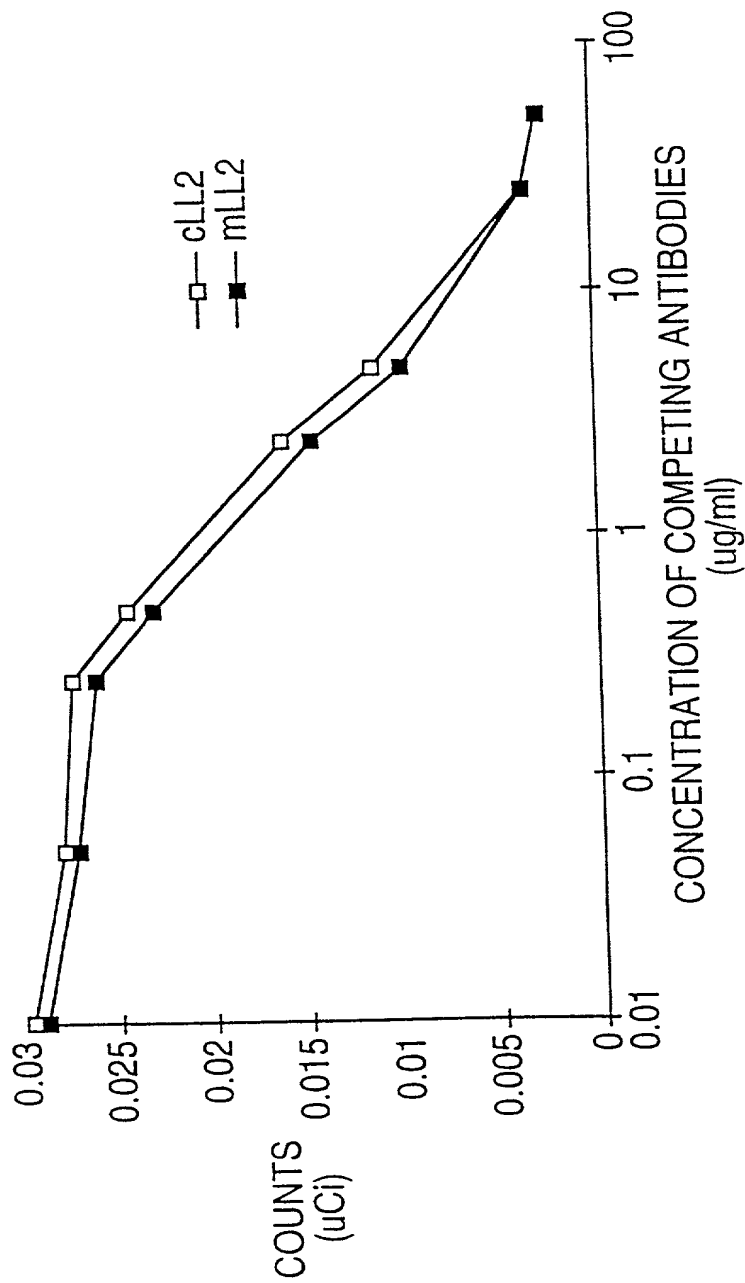


FIG. 11A

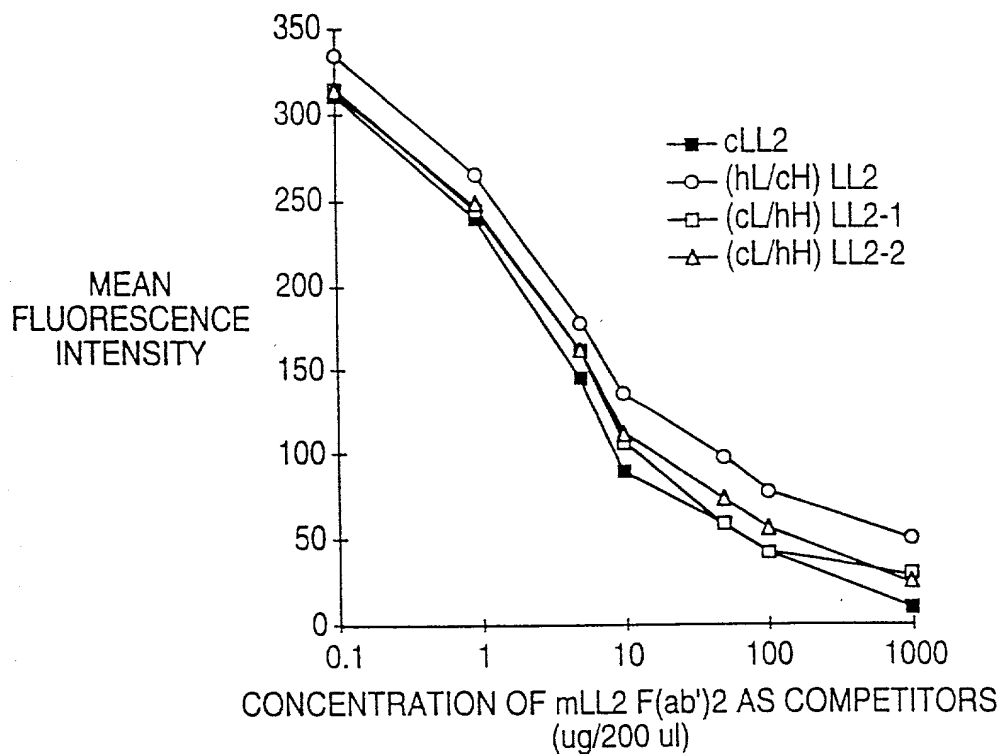


FIG. 11B

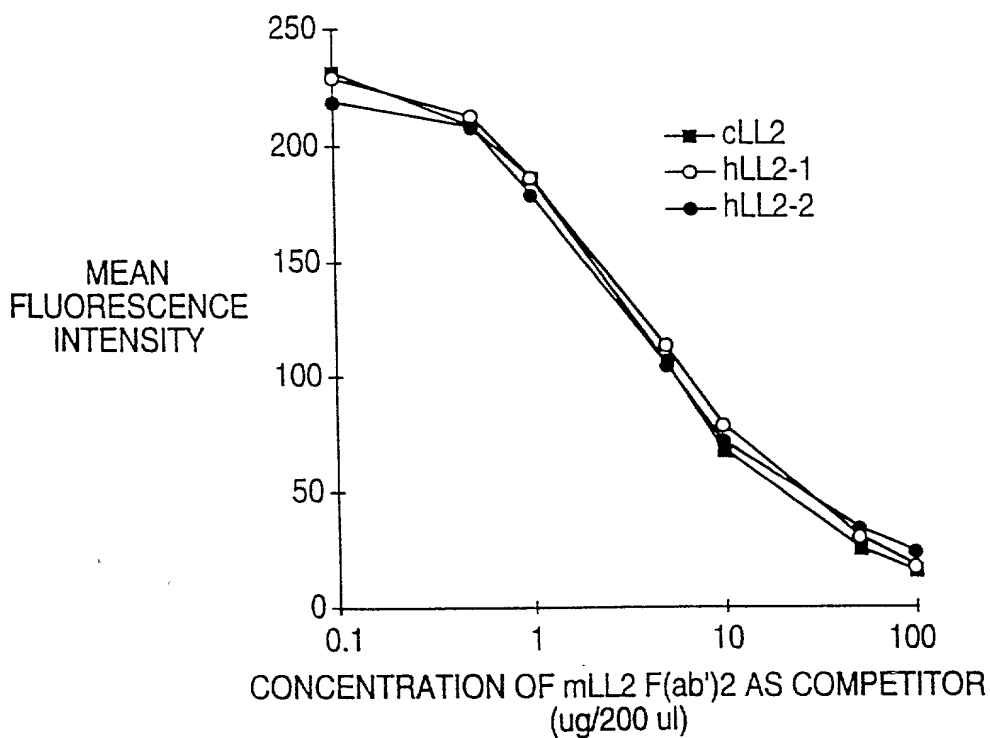


FIG. 12

INTERNALIZATION: c-LL2, h-LL2 vs. m-LL2 IN RAJI CELLS

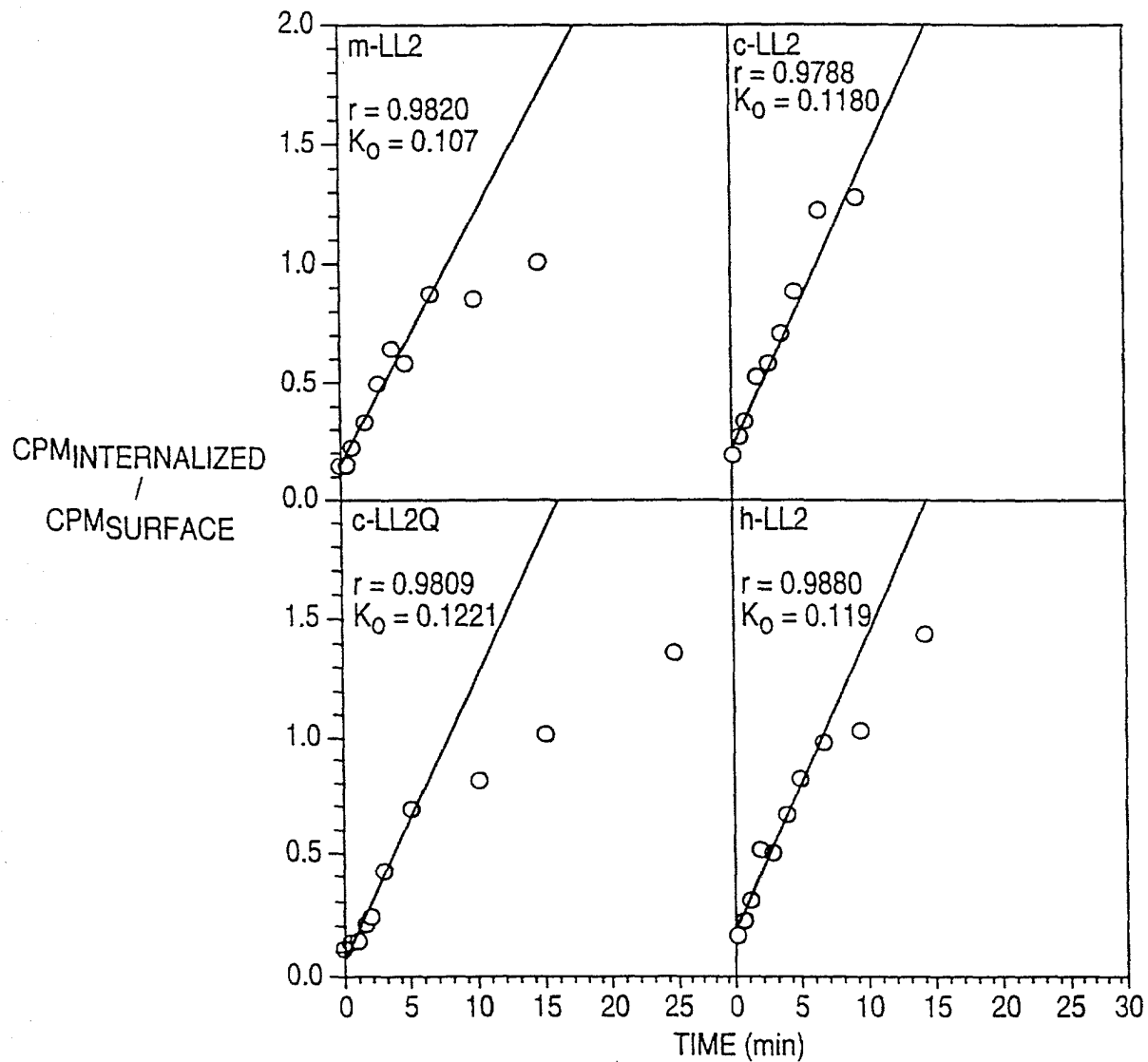


FIG. 13

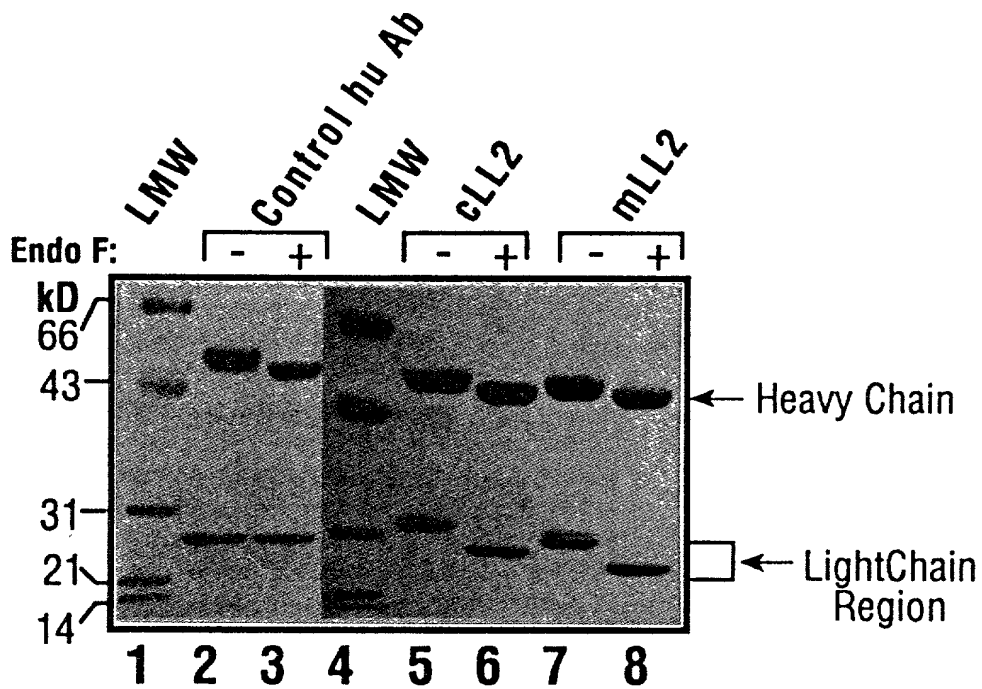


FIG. 14

